



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

6. Xiang M, Zhang Z, Kuwahara K. Impact of COVID-19 pandemic on children and adolescents' lifestyle behavior larger than expected. *Prog Cardiovasc Dis*. 2020;63(4):531–532.



Comparison of Myopic Progression before, during, and after COVID-19 Lockdown



Coronavirus disease 2019 (COVID-19) is an emerging infectious disease against which lockdown has been applied widely as a policy to stop its spread. Although many people believe that myopic progression has accelerated during the COVID-19 pandemic lockdown, evidence to support this presumption is lacking.

The Myopia Screening Survey of Children and Teenagers in Schools is a cohort study conducted in 46 primary and junior high schools in Hangzhou, China. As shown in Figure S1 (available at www.aaojournal.org), the first participants were examined in early 2019, with examinations performed at approximately 6-month intervals thereafter. By now, 4 rounds (referred to as rounds 1–4) of the survey have been completed, with 3 periods (referred to as periods 1–3) between them. The COVID-19 lockdown was implemented during period 2. This study was approved by the ethics committee of the Eye Hospital of Wenzhou Medical University (identifier, 2019-083-K-80), and the study adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from all the participants and their parents or guardians. The study is supported by the National Natural Science Foundation of China (Grant No.81830027).

The presenting visual acuity (VA) was defined as corrected VA in students with glasses and uncorrected VA in others. Refractive error was estimated by noncycloplegic autorefractometer with a Tianle RM9000 autorefractometer (Ningbo Ming Sing Optical R&D Co, Ltd). The spherical equivalent refraction (SER) was calculated as sphere power +0.5 × cylinder power. Myopia of one eye was defined as SER of −0.5 diopter (D) or less, and high myopia was defined as SER of −6.0 D or less.¹ If either eye of a student was myopic or highly myopic, the student was defined as having myopia or high myopia. Myopic progression was defined as a more negative SER in the same eye. The rate of SER change (rΔSER) was calculated as the difference in SER divided by the corresponding interval in months. Age was calculated in days and was analyzed as a continuous variable. Both age and age squared were adjusted in Tables S1 and S2 (available at www.aaojournal.org) because nonlinear associations between the analyzed variables (SER, myopic proportion, and rΔSER) and age were found (Fig 1B–D).

As shown in Figure S2 (available at www.aaojournal.org), of the 44 187 students at baseline, 29 719 (59 438 eyes) were included in the analyses. In Table S3 (available at www.aaojournal.org), the proportions of myopia and high myopia at rounds 1 through 4 were 48.0%, 53.2%, 73.7%, and 67.9% and 1.3%, 1.9%, 2.8%, and 2.7% respectively, which showed a general upward trend, with a slight decrease at round 4. The mean rΔSER during periods 1, 2, and 3 was −0.030 D/month (95% confidence interval [CI], −0.031 to −0.029 D/month), −0.074 D/month (95% CI, −0.075 to −0.074 D/month), and 0.016 D/month (95% CI, 0.015–0.018 D/month). The changes in the refractive state were supported by the SER distribution in Figure 1A,

revealing negative deviations at rounds 2 and 3 and a positive shift at round 4.

In Table S2, compared with round 1, the covariate-adjusted (age, age squared, and gender) differences in myopic proportion and SER were not significant at round 2 ($P = 0.162$ and $P = 0.195$) but were significant at rounds 3 and 4 ($P < 0.001$); for high myopia, a significant increase at round 3 was found ($P < 0.001$). Younger age and male gender were associated with a lower risk of myopia. Consistent with Table S2, in Figure 1B, C, the distribution plots for myopia prevalence and SER of rounds 1 and 2 almost coincided, whereas the round 3 curves were remarkably more myopic, the round 4 curves were between the round 2 and 3 curves, and the differences among different rounds were more remarkable in younger students.

In model I of Table S1, compared with period 1, the covariates (age, age squared, gender, SER, and presenting VA) adjusted rΔSER was significantly more negative during period 2 and more positive during period 3 ($P < 0.001$). If periods 2 and 3 were considered as 1 period in calculations (model II), the mean rΔSER was more negative than that during period 1 (difference, −0.009 D/month; 95% CI, −0.010 to −0.008 D/month; $P < 0.001$). Table S1 also indicates a better presenting VA related to slower myopic progression in all models ($P < 0.001$). As shown in Figure 1D, the difference in rΔSER across the 3 survey periods was more remarkable in younger students, which indicates that younger participants were more sensitive to lockdown with regard to myopic progression.

The rate of myopic progression was greater during period 2, followed by an interestingly hyperopic progression during period 3. We speculate that this may be explained by accommodative spasm during lockdown. Corneal power, axial length, and ocular accommodation are the 3 vital factors in the refractive state. Corneal power is usually stable after 2 years of age in children,² and currently it is believed that reduction in axial length does not occur. During the COVID-19 lockdown, the restricted outdoor time, increased screen time,³ and limited indoor space (in Hangzhou, most families reside in multistory apartment buildings) may have caused accommodative spasm in the students, which could present as increased myopic progression. At round 4, which was approximately half a year after the lockdown was lifted, the accommodative spasm reversed, and the refractive state consequently became more hyperopic. Model II of Table S1 indicates that myopic progression was greater, even allowing for the effect of accommodative spasm. We attempted to remove the effect of temporary accommodative spasm by considering periods 2 and 3 as 1 period in our calculations. The data suggest that both reversible accommodative spasm and permanent structural changes contributed to the greater rate of myopia progression during lockdown. Before our study, outdoor time had been investigated as a protective factor for myopia⁴; theories to explain the underlying mechanism are focused mainly on light exposure and dopamine levels.⁵ We found that younger participants are more susceptible to myopic progression during lockdown. Two possible hypotheses for this age-related difference, are as follows. The first is that lifestyle changes were less pronounced in older students during lockdown. This theory is supported by a nationwide survey in China that the outdoor time decreased with more school years before college.⁶ The second is that younger participants may be more sensitive to the

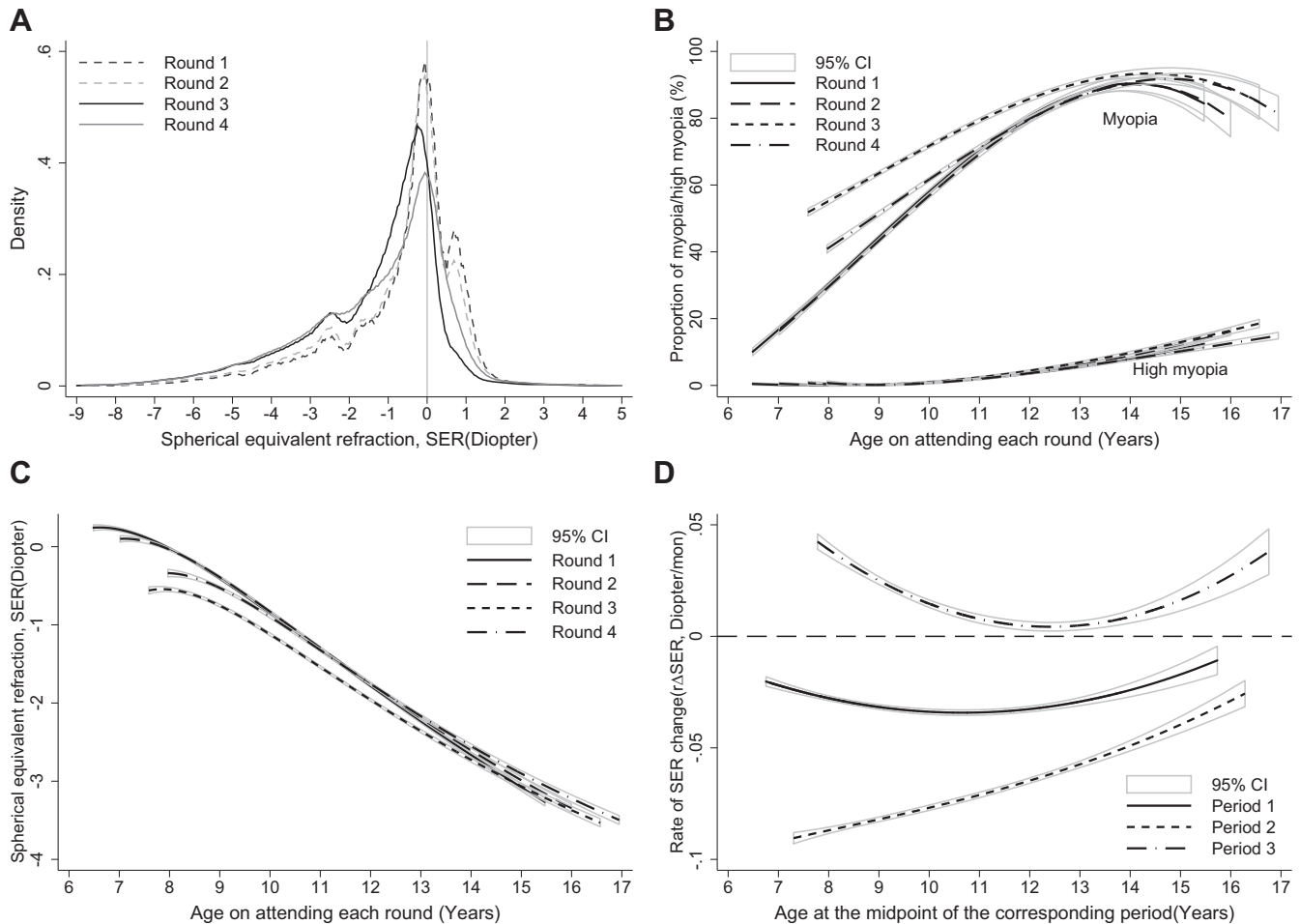


Figure 1. Line graphs showing the cross-sectional distribution of (A) the refractive state at each survey round, (B) the proportions of myopia and high myopia by age at each survey round, (C) the spherical equivalent refraction (SER) by age at each survey round, and (D) the age curves of the rate of SER change during each survey period. The curves in (A) are smoothed with kernel density estimates, and the curves in (B–D) are smoothed with fractional-polynomial prediction. CI = confidence interval.

lifestyle changes during the lockdown with regard to myopic progression.

Currently, evidence is limited concerning whether social policies can affect myopic progression. In Singapore, the prevalence of myopia among primary school students decreased after the National Myopia Prevention Program was implemented.⁷ Our study indicates that lockdown, as a social policy, can alter refractive state in a partially reversible manner.

The large sample size and longitudinal follow-up are the major strengths of our study. Although the influence of accommodation may bias the outcomes, biometric examinations were not performed. Moreover, caution must be exercised when interpreting evidence in other populations who live in other areas.

In conclusion, our study indicates accelerated myopic progression during the COVID-19 pandemic lockdown in children and teenagers. However, this myopic progression was reversed partially after lockdown, suggesting that both accommodative spasm and structural changes contributed to this accelerated rate. Myopic progression should be considered and managed when a lockdown is imposed in the future.

Acknowledgment

The authors thank the students who participated in this survey.

PINGJUN CHANG, MD^{1,2,*}

BING ZHANG, MD^{1,2,*}

LI LIN, MD^{1,2}

RURU CHEN, MD^{1,2}

SIPING CHEN, MD^{1,2}

YUNE ZHAO, MD^{1,2}

JIA QU, MD^{1,2}

¹Eye Hospital and School of Ophthalmology and Optometry, Wenzhou Medical University, Wenzhou, Zhejiang, China; ²National Clinical Research Center for Ocular Diseases, Wenzhou, Zhejiang, China

*Both authors contributed equally as first authors.

Disclosure(s):

All authors have completed and submitted the ICMJE disclosures form. The author(s) have no proprietary or commercial interest in any materials discussed in this article.

Supported by the National Natural Science Foundation of China (grant no.: 81830027). No funders had a direct role in the collection, management, analysis, or interpretation of the data; preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication.

HUMAN SUBJECTS: Human subjects were included in this study. This study was approved by the ethics committee of the Eye Hospital of Wenzhou Medical University. All research adhered to the tenets of the Declaration of Helsinki. All participants and their parents or guardians provided informed consent.

No animal subjects were used in this study.

Author Contributions:

Conception and design: Chang, Zhang, Zhao, Qu

Analysis and interpretation: Chang, Zhang, Lin, R.Chen, S.Chen, Zhao, Qu

Data collection: Chang, Qu

Obtained funding: N/A

Overall responsibility: Qu, Zhao, Chang, Zhang, Lin, R.Chen, S.Chen

Keywords:

Children and teenagers, Chinese students, Community containment, COVID-19, Lockdown, Myopia, Myopic progression, Presenting visual acuity, Refractive error, Reopening, Social policy.

Correspondence:

Yune Zhao, MD, Zhejiang Eye Hospital, Fengqidong Road No. 618, Hangzhou, Zhejiang, China, 310020. E-mail: zyehzeye@126.com; and Jia Qu, MD, 270 Xueyuan Road, Wenzhou, Zhejiang, China, 325027. E-mail: jia.qu@163.com.

References

1. Flitcroft DI, He M, Jonas JB, et al. IMI—defining and classifying myopia: a proposed set of standards for clinical and epidemiologic studies. *Invest Ophthalmol Vis Sci*. 2019;60(3):M20–M30.
2. Mutti DO, Sinnott LT, Lynn Mitchell G, et al. Ocular component development during infancy and early childhood. *Optom Vis Sci*. 2018;95(11):976–985.
3. Xiang M, Zhang Z, Kuwahara K. Impact of COVID-19 pandemic on children and adolescents' lifestyle behavior larger than expected. *Prog Cardiovasc Dis*. 2020;63(4):531–532.
4. He M, Xiang F, Zeng Y, et al. Effect of time spent outdoors at school on the development of myopia among children in China: a randomized clinical trial. *JAMA*. 2015;314(11):1142–1148.
5. Hysi PG, Choquet H, Khawaja AP, et al. Meta-analysis of 542,934 subjects of European ancestry identifies new genes and mechanisms predisposing to refractive error and myopia. *Nat Genet*. 2020;52(4):401–407.
6. Xu R-B, Gao D, Wang Z-H, et al. Analysis of the current status of outdoor activity time of Chinese students in 2016. *Chinese Journal of Child Health Care*. 2018;26(03):254–257.
7. Karuppiiah V, Wong L, Tay V, et al. School-based programme to address childhood myopia in Singapore. *Singapore Med J*. 2021;62(2):63–68.



Association of Early Anatomic Response with Visual Function in Neovascular Age-Related Macular Degeneration



Patients with neovascular age-related macular degeneration (nAMD) experience impaired visual acuity (VA), with some also reporting a loss of vision-related functions affecting activities such as reading, writing, and driving.¹ Clinical treatment of nAMD is commonly guided by OCT, which gives information on retinal thickness and fluid location, typically in combination with vision measurement. However, there is often no or poor correlation between retinal thickness and vision,² and neither of the assessments incorporate vision-related function changes into the criteria used for retreatment. Furthermore, the relationship between vision-related functions and fluid location has been less characterized than the relationship between vision and fluid location, and the impact of a less than complete dryness response to anti-vascular endothelial growth factor (VEGF) therapy on subsequent vision and vision-related function outcomes is unknown. In this integrated analysis of the Vascular Endothelial Growth Factor VEGF Trap-Eye: Investigation of Efficacy and Safety in Wet AMD (VIEW) trials,³ we assessed whether early persistent retinal dryness in response to anti-VEGF therapy translates into vision-related function and/or VA benefit.

Each clinical site's respective institutional review board or ethics committee approved the study protocol. All patients provided written informed consent. The VIEW trials adhered to the ethical guidelines of the Declaration of Helsinki and the Health Insurance Portability and Accountability Act.

Of the 2412 eyes in the full analysis set of the VIEW trials, this analysis included 1815 eyes with known retinal fluid status from baseline through week 12 that were treated with 0.5 mg intravitreal ranibizumab every 4 weeks (Rq4; n = 595), 2 mg intravitreal aflibercept injection (IAI) every 4 weeks (2q4; n = 613), or 2 mg IAI every 8 weeks after 3 initial monthly doses (2q8; n = 607). Eyes were categorized into 2 subgroups based on qualitative status of retinal fluid at the first 3 visits (weeks 4, 8, and 12) after initiation of treatment: eyes with no retinal fluid (persistently dry [PD]) and eyes with retinal fluid at 1 or more visit (not persistently dry [NPD]). Changes from baseline through week 24 in vision-related function (combined treatment groups) and best-corrected VA (BCVA; both combined and individual treatment groups) were evaluated by anatomic location of fluid: intraretinal fluid (IRF), subretinal fluid (SRF), and overall retinal fluid (ORF). Vision-related function was assessed using the 25-item National Eye Institute Visual Function Questionnaire (NEI-VFQ-25) at baseline and weeks 12 and 24. A difference of 5 points or more in the NEI-VFQ-25 score was considered a clinically significant change.⁴ Best-corrected VA was measured by an Early Treatment Diabetic Retinopathy Study chart every 4 weeks through week 24.